

IT IS CLAIMED:

1. A pharmaceutical composition, comprising an agent effective to induce an immune response against an amyloid component in a patient, and a pharmaceutical excipient.
- 5 2. The pharmaceutical composition of claim 1, wherein the amyloid component is a fibril peptide or protein.
3. The pharmaceutical composition of claim 2, wherein the amyloid component is derived from a fibril precursor protein selected from the group consisting of proteins or peptides consisting of Serum Amyloid A protein (ApoSSA), immunoglobulin light chain, 10 immunoglobulin heavy chain, ApoAI, transthyretin, lysozyme, fibrogen α chain, gelsolin, cystatin C, Amyloid β protein precursor (β -APP), Beta₂ microglobulin, prion precursor protein (PrP), atrial natriuretic factor, keratin, islet amyloid polypeptide, a peptide hormone, and synuclein; including mutant proteins, protein fragments and proteolytic peptides thereof.
- 15 4. The pharmaceutical composition of claim 3, wherein said agent induces an immune response directed against a neoepitope formed by said fibril protein or peptide, with respect to a fibril precursor protein.
5. The pharmaceutical composition of claim 3, wherein said amyloid component is selected from the group consisting of AA, AL, ATTR, AApoA1, Alys, Agel, Acys, A β , 20 AB₂M, AScr, Acal, AIAPP and synuclein-NAC fragment.
6. The pharmaceutical composition of claim 5, wherein said agent is selected from the group consisting of AA, AL, ATTR, AApoA1, Agel, Acys, A β , AB₂M, AScr, Acal, AIAPP and synuclein-NAC fragment.
7. The pharmaceutical composition of claim 1, wherein said composition comprises 25 an agent effective to induce an immunogenic response against at least two different amyloid components.
8. The pharmaceutical composition of claim 1, wherein said agent is a peptide linked to a carrier protein.

9. The pharmaceutical composition of any of claims 1 to 8, wherein the composition includes an adjuvant.

10. The pharmaceutical composition of claim 9, wherein said adjuvant is selected from the group consisting of QS21, monophosphoryl lipid, alum and Freund's adjuvant.

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5 11. A method of preventing or treating a disorder characterized by amyloid deposition in a mammalian subject, comprising administering to the subject a dosage of an agent effective to produce an immune response against an amyloid component characteristic of said disorder.

10 12. The method of claim 11, wherein said amyloid component is a fibril protein or peptide.

13. The method of claim 12, wherein said immune response is directed to fibril component derived from a precursor protein selected from the group consisting of Serum Amyloid A protein (ApoSSA), immunoglobulin light chain, immunoglobulin heavy chain, ApoAI, transthyretin, lysozyme, fibrogen α chain, gelsolin, cystatin C, Amyloid β protein precursor (β -APP), Beta₂ microglobulin, prion precursor protein (PrP), atrial natriuretic factor, keratin, islet amyloid polypeptide, a peptide hormone, and synuclein; including mutant proteins, protein fragments or peptides thereof.

20 14. The method of claim 13, wherein said agent induces an immune response directed against a neoepitope formed by said amyloid component with respect to said precursor protein.

15. The method of claim 13, wherein said amyloid component is selected from the group consisting of AA, AL, ATTR, AapoA1, Alys, Agel, Acys, A β , AB₂M, AScr, Acal, AIAPP and synuclein-NAC fragment.

25 16. The method of claim 15, wherein said agent is selected from the group consisting of AA, AL, ATTR, AapoA1, Agel, Acys, A β , AB₂M, AScr, Acal, AIAPP and synuclein-NAC fragment.

17. The method of claim 11, wherein said agent is effective to induce an immunogenic response against at least two different amyloid components.

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18. The method of claim 17, wherein said administering includes administering at least two amyloid fibril components.

19. The method of claim 11, wherein said agent is a peptide linked to a carrier protein.

20. The method of any of claims 11-19, wherein said administering further includes 5 an adjuvant.

21. The method of claim 20, wherein said adjuvant is selected from the group consisting of QS21, monophosphoryl lipid, alum and Freund's adjuvant.

22. The method of claim 11, wherein said immunological response is characterized by a serum titer of at least 1:1000 with respect to said amyloid component.

10 23. The method of claim 22, wherein said serum titer is at least 1:5000 with respect to said fibril component.

24. The method of claim 11, wherein said immunological response is characterized by a serum amount of immunoreactivity corresponding to greater than about four times higher than a serum level of immunoreactivity measured in a pre-treatment control serum 15 sample.

25. The method of claim 24, wherein said serum amount of immunoreactivity is measured at a serum dilution of about 1:100.

26. A method of determining the prognosis of a patient undergoing treatment for an amyloid disorder, comprising measuring a patient serum amount of immunoreactivity 20 against a selected amyloid component, wherein a patient serum amount of immunoreactivity of at least four times a baseline control level of serum immunoreactivity is indicative of a prognosis of improved status with respect to said disorder.

27. The method of claim 26, wherein said patient serum amount of immunoreactivity 25 against said selected amyloid component is characterized by a serum titer of at least about 1:1000.

28. The method of claim 27, wherein said patient serum amount of immunoreactivity against said selected amyloid component is characterized by a serum titer of at least 1:5000.

29. A method of preventing or treating a disease characterized by an amyloid deposit in a patient, comprising administering to said patient an effective dosage of an antibody or antibody fragment that specifically binds to an amyloid component present in said deposit.

30. The method of claim 29, wherein said amyloid component is a fibril component.

31. The method of claim 30, wherein said antibody or antibody fragment binds to an epitope of said fibril component.

32. The method of claim 31, wherein the antibody or antibody fragment specifically binds to said fibril component without binding to a precursor of said fibril component.

33. The method of claim 30, wherein the antibody is a human antibody to said fibril component prepared from B cells from a human immunized with a fibril component epitope.

34. The method of claim 30, wherein said amyloid fibril component is derived from a precursor protein selected from the group consisting of Serum Amyloid A protein (ApoSSA), immunoglobulin light chain, immunoglobulin heavy chain, ApoAI, transthyretin, lysozyme, fibrogen α chain, gelsolin, cystatin C, Amyloid β protein precursor (β -APP), Beta $_2$ microglobulin, prion precursor protein (PrP), atrial natriuretic factor, keratin, islet amyloid polypeptide, a peptide hormone, and synuclein; including mutant proteins, protein fragments or peptides thereof.

35. The method of claim 34, wherein said amyloid fibril component is selected from the group consisting of AA, AL, ATTR, AapoA1, Alys, Agel, Acys, A β , AB $_2$ M, AScr, Acal, AIAPP and synuclein-NAC fragment.

36. The method of claim 29, wherein said administering includes administering antibodies which bind at least two amyloid fibril components.

37. The method of claim 29, wherein said effective dosage is characterized by a level in the patient of a serum amount of immunoreactivity against said amyloid component that is at least about four times higher than a serum level of immunoreactivity against said component measured in a pre-treatment control serum sample.

5 38. The method of claim 29, wherein the antibody or antibody fragment is administered with a carrier as a pharmaceutical composition.

39. The method of claim 29, wherein the antibody or antibody fragment is administered intraperitoneally, orally, subcutaneously, intramuscularly, intranasally, topically or intravenously.

10 40. The method of claim 29, wherein the antibody is administered by administering a polynucleotide encoding at least one antibody chain to the patient, and wherein the polynucleotide is expressed to produce the antibody chain in the patient.

41. The method of claim 40, wherein the polynucleotide encodes heavy and light chains of the antibody, which polynucleotide is expressed to produce the heavy and light 15 chains in the patient.

42. The method of claim 29, wherein the antibody or antibody fragment is administered in multiple dosages over a period of at least six months.

43. The method of claim 29, wherein the antibody is administered as a sustained release composition.

20 44. A pharmaceutical composition for preventing or treating a disease characterized by an amyloid deposit in a patient, comprising an effective dosage of an antibody or antibody fragment that specifically binds to an amyloid component present in said deposit.

45. The pharmaceutical composition of claim 44, wherein said amyloid component is 25 a fibril component.

46. The pharmaceutical composition of claim 45, wherein said antibody binds to an epitope of said fibril component.

47. The pharmaceutical composition of claim 46, wherein the antibody specifically binds to said fibril component without binding to a precursor of said fibril component.

5 48. The pharmaceutical composition of claim 46, wherein the antibody is a human antibody to said fibril component prepared from B cells from a human immunized with a fibril component epitope.

49. The pharmaceutical composition of claim 45, wherein said amyloid fibril component is derived from a precursor protein selected from the group consisting of

10 Serum Amyloid A protein (ApoSSA), immunoglobulin light chain, immunoglobulin heavy chain, ApoAI, transthyretin, lysozyme, fibrogen α chain, gelsolin, cystatin C, Amyloid β protein precursor (β -APP), Beta₂ microglobulin, prion precursor protein (PrP), atrial natriuretic factor, keratin, islet amyloid polypeptide, a peptide hormone, and synuclein; including mutant proteins, protein fragments or peptides thereof.

15 50. The pharmaceutical composition of claim 49, wherein said amyloid fibril component is selected from the group consisting of AA, AL, ATTR, ApoA1, Alys, Agel, Acys, A β , AB₂M, AScr, Acal, AIAPP and synuclein-NAC fragment.

51. The pharmaceutical composition of claim 44, wherein said composition includes antibodies or antibody fragments which bind at least two amyloid fibril components.

20 52. The pharmaceutical composition of claim 44, wherein said effective dosage is characterized by an amount of antibody or antibody fragment effective to produce a level in the patient serum of immunoreactivity against said amyloid component that is at least about four times higher than a serum level of immunoreactivity against said component measured in a pre-treatment control serum sample.

25 53. The pharmaceutical composition of claim 44, wherein the pharmaceutical composition includes a carrier.

54. The pharmaceutical composition of claim 44, wherein the pharmaceutical composition is formulated for administration intraperitoneally, orally, subcutaneously, intramuscularly, intranasally, topically or intravenously.

55. The pharmaceutical composition of claim 44, wherein the pharmaceutical composition includes a polynucleotide encoding at least one antibody chain effective to express the antibody chain in the patient.

56. The pharmaceutical composition of claim 55, wherein the polynucleotide encodes heavy and light chains of the antibody, which polynucleotide is capable of expression to produce the heavy and light chains in the patient.

10 57. The pharmaceutical composition of claim 44, wherein said pharmaceutical composition is formulated as a sustained release composition.